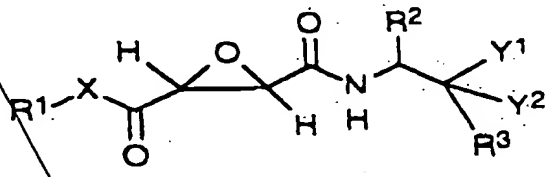
-- 22. An epoxysuccinamide derivative having the following formula (1) and its physiologically acceptable salt:



(1)

wherein

R^1 represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, ~~a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms~~;

R^2 represents an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, ~~a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms~~;

R^3 represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10

contd.
A1

carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

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X represents -O- or -NR^4- in which R^4 is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

Y^1 represents a hydroxyl group, an alkoxy group having 1 to 6 carbon atoms, an acetoxy group, or an aralkyloxy group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms; and

Y^2 represents a hydrogen atom or an alkyl group having 1 to 10 carbon atoms;

provided that ~~each of~~ the aryl group ~~and the heterocyclic group~~ for R^1 to R^4 may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino.

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contd.
a1

23. The epoxysuccinamide derivative of the formula (1) and its physiologically acceptable salt defined in claim 22, wherein R^1 is a hydrogen atom or an alkyl group having 1 to 6 carbon atoms.

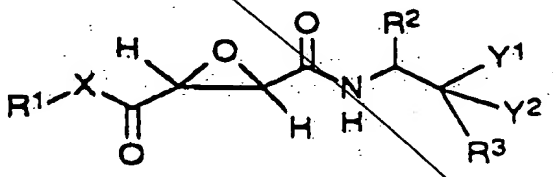
24. The epoxysuccinamide derivative of the formula (1) and its physiologically acceptable salt defined in claim 22, wherein R^2 is an alkyl group having 1 to 6 carbon atoms, phenyl, or benzyl.

25. The epoxysuccinamide derivative of the formula (1) and its physiologically acceptable salt defined in claim 22, wherein R^3 is a hydrogen atom or an aryl group having 6 to 20 carbon atoms.

26. The epoxysuccinamide derivative of the formula (1) and its physiologically acceptable salt defined in claim 22, wherein X is -O-.

27. The physiologically acceptable salt of the epoxysuccinamide derivative defined in claim 22, wherein the physiologically acceptable salt is an alkali metal salt.

28. An epoxysuccinamide derivative having the following formula (1) and its physiologically acceptable salt:



(1)

wherein

R^1 represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10

57 B

contd.

carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, ~~or a heterocyclic alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms~~;

R^2 represents an isobutyl group or an isopropyl group;

R^3 represents a hydrogen atom or an aryl group having 6 to 20 carbon atoms;

X represents -O- or $-NR^4-$ in which R^4 is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

Y^1 represents OR^5 in which R^5 is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, an acyl group having 2 to 20 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms; and

Y^2 represents a hydrogen atom;

provided that the alkyl group for R^5 may have one or more substituents selected from the group consisting of hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, carboxyl, alkoxycarbonyl having

contd A1

2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, and guanidino, and

provided that ~~each of~~ the aryl group ~~and the heterocyclic group~~ for R^1, R^3 and R^5 may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino.

B2 C1 Cont

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~~29~~. The epoxysuccinamide derivative of the formula (1) and its physiologically acceptable salt defined in claim ~~28~~ 7, wherein R^1 is a hydrogen atom or an alkyl group having 1 to 6 carbon atoms.

9
~~30~~. The epoxysuccinamide derivative of the formula (1) and its physiologically acceptable salt defined in claim ~~28~~ 7, wherein X is -O-.

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~~31~~. The physiologically acceptable salt of the epoxysuccinamide derivative defined in claim ~~28~~ 7, wherein the physiologically acceptable salt is an alkali metal salt.

Sub D3

32. A method for treating bone diseases which comprises injecting or orally administering into a patient an epoxysuccinamide derivative having the following formula (1) and its physiologically acceptable salt in an amount of 0.01 to 100 mg/day in the case of injection or in an amount of 0.1 mg/day to 1 g/day in the case of oral administration:

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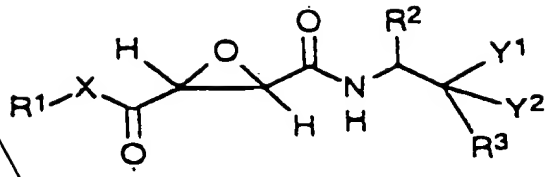

(1)

Sub D3

wherein

R^1 represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, or an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, ~~a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms~~;

R^2 represents an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, ~~a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms~~;

R^3 represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms,

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contd. A1

Sub D3

a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

X represents -O- or -NR^4- in which R^4 is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

Y^1 represents a hydroxyl group, an alkoxy group having 1 to 6 carbon atoms, an acetoxy group, or an aralkyloxy group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms; and

Y^2 represents a hydrogen atom or an alkyl group having 1 to 10 carbon atoms;

provided that each of the aryl group and the heterocyclic group for R^1 to R^4 may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino.

33. A method for treating arthritis which comprises injecting or orally administering into a patient an epoxysuccinamide derivative having the following formula (1) and its physiologically acceptable salt in an amount

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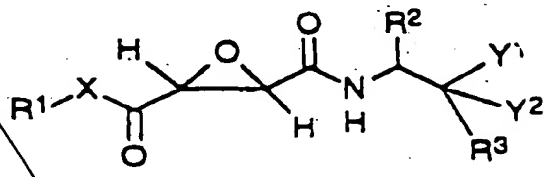
of 0.01 to 100 mg/day in the case of injection or in an amount of 0.1 mg/day to 1 g/day in the case of oral administration:



(1)

wherein

R^1 represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, ~~a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms~~;

R^2 represents an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, ~~a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms~~;

R^3 represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an ar-

contd. A1

alkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

Sub D3

X represents -O- or -NR^4- in which R^4 is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

Y^1 represents a hydroxyl group, an alkoxy group having 1 to 6 carbon atoms, an acetoxy group, or an aralkyloxy group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms; and

Y^2 represents a hydrogen atom or an alkyl group having 1 to 10 carbon atoms;

provided that each of the aryl group and the heterocyclic group for R^1 to R^4 may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino.

Rule C2

34. A method for treating bone diseases which comprises injecting or orally administering into a patient

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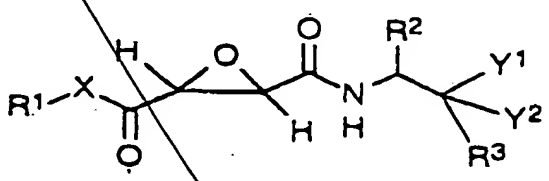
an epoxysuccinamide derivative having the following formula (1) and its physiologically acceptable salt in an amount of 0.01 to 100 mg/day in the case of injection or in an amount of 0.1 mg/day to 1 g/day in the case of oral administration:



(1)

wherein

R^1 represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, ~~a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms~~;

R^2 represents an isobutyl group or an isopropyl group;

R^3 represents a hydrogen atom or an aryl group having 6 to 20 carbon atoms;

X represents -O- or $-NR^4-$ in which R^4 is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon

contd. A1

atoms;

Y^1 represents OR^5 in which R^5 is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, an acyl group having 2 to 20 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms; and

C2 cont

Y^2 represents a hydrogen atom;

provided that the alkyl group for R^5 may have one or more substituents selected from the group consisting of hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, and guanidino, and

B3

provided that ~~each of~~ the aryl groups ~~and the heterocyclic groups~~ for R^1, R^3 and R^5 may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino.

35. A method for treating arthritis which comprises injecting or orally administering into a patient an epoxysuccinamide derivative having the following formula (1) and its physiologically acceptable salt in an amount of 0.01 to 100 mg/day in the case of injection or in an

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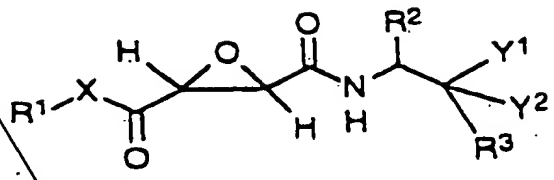
amount of 0.1 mg/day to 1 g/day in the case of oral administration:



(1)

wherein

R^1 represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, ~~a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms~~;

R^2 represents an isobutyl group or an isopropyl group;

R^3 represents a hydrogen atom or an aryl group having 6 to 20 carbon atoms;

X represents -O- or $-NR^4-$ in which R^4 is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

Y^1 represents OR^5 in which R^5 is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising

an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, an acyl group having 2 to 20 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms; and

Y^2 represents a hydrogen atom;

provided that the alkyl group for R^5 may have one or more substituents selected from the group consisting of hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, and guanidino, and

provided that ~~each of~~ the aryl groups ~~and the heterocyclic groups~~ for R^1, R^3 and R^5 may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino.

~~16.~~ An epoxysuccinamide derivative selected from the group consisting of the following compounds and its physiologically acceptable salt:

ethyl (2S,3S)-3-[[1-(S)-benzoyl-3-methylbutyl]-carbamoyl]oxirane-2-carboxylate;

ethyl (2S,3S)-3-[[1-(S)-benzoyl-2-methylpropyl]-carbamoyl]oxirane-2-carboxylate;

ethyl (2S,3S)-3-[[1-(S)-(benzoylamino)methyl-3-methylbutyl]carbamoyl]oxirane-2-carboxylate;

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ethyl (2S,3S)-3-[[1-(S)-(2-methyl-2-propenyloxy)-methyl-3-methylbutyl]carbamoyl]oxirane-2-carboxylate;

ethyl (2S,3S)-3-[[1-(S)-(hexanoylamino)methyl-3-methylbutyl]carbamoyl]oxirane-2-carboxylate;

sub c' cont

ethyl (2S,3S)-3-[[1-(S)-(N-benzyl-N-methylamino)-methyl-3-methylbutyl]carbamoyl]oxirane-2-carboxylate;

and,

ethyl (2S,3S)-3-[[1-(S)-(N-hexyl-N-methylamino)-methyl-3-methylbutyl]carbamoyl]oxirane-2-carboxylate. --

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